REMARKS

Reconsideration of this application is respectfully requested.

Claims 1-72 are pending in the application. Claims 29-31, 37-45 and 59-66 are withdrawn from consideration as being drawn to non-elected inventions. Claims 1-7, 13-18, 32-33, and 52-54 have been canceled without prejudice or disclaimer. Claims 8-12, 19-28, 34-36, 46-58 and 67-72 are rejected. Claims 8, 10, 12, 19, 21, 22, 25, 27, 34, 46, 47, 50 and 57 have been amended to better clarify what Applicants regard as the invention. Support for the amendments can be found throughout the specification, in particular on page 13, lines 10-28, continuing onto page 14, lines 1-3 and in the claims as originally filed. Support for new claims 73 and 74 can be found throughout the specification, but particularly in Example 3. No new matter has been added by way of this amendment. Thus, as a result of the foregoing amendment, claims 8-12, 19-28, 34-36, 46-51, 55-58 and 67-74 are under consideration.

Claim Rejections under 35 U.S.C. §112, first paragraph

Claims 8-12, 19-28, 34-36, 46-58 and 67-72 are rejected under 35 U.S.C. §112, first paragraph for lack of enablement. More particularly, the Examiner alleges that the specification, while being enabled for "increasing neural expression of eNCAM, MAP II, beta-tubulin, nestin, NF or NF-PO4" with the administration of N-[4-[(3-fluorophenyl)sulfonyl]phenyl]acetamide or "treating spinal cord injury by administering bone marrow cells from N-[4-[(4-fluorophenyl)sulfonyl]phenyl]acetamide-treated animals to a site of injury in an animal, does not reasonably provide enablement for "promoting neural tissue regeneration or expression", "promoting recovery of behavioral function of neurons", "treating injury to neural tissue", "inducing neuronal replacement for treating a neurodegenerative conditions or disease" and "promoting regeneration of neural precursor cells", with the administration of compounds of formula II. The Examiner alleges that the specification does not enable a person skilled in the art to practice the invention commensurate in scope with the claims. Furthermore, the Examiner alleges that one skilled in the art could not practice the invention without undue experimentation.

Applicants respectfully traverse the Examiner's rejection and have amended the claims to better clarify the invention. Furthermore, Applicants provide herewith a declaration under 37 CFR 1.132 which provides additional data in support of enablement of the invention as currently claimed.

More particularly, Applicants have amended the claims to recite: "...method for promoting neural cell growth or differentiation by administering..." and furthermore, "...administering is sufficient to induce a detectable increase in neural expression of one or more proteins indicative of neural cell growth or differentiation." Further claim amendments include "method for promoting recovery of cells expressing neuronal progenitor cell markers after injury to the neuronal cells...". In addition, some proteins that are indicative of neural cell growth or differentiation are selected from the group consisting of eNCAM, MAP II, beta tubulin, nestin, NF and NF-PO4. Applicants respectfully point out to the Examiner that while other proteins may be known to be associated with neural precursor cells, the proteins utilized in these studies are representative of the proteins that are expressed by neuronal precursor cells during the early stages of differentiation from a neural stem cell before maturation into an adult neural cell. Accordingly, these proteins are reflective of the growth and differentiation of neuronal precursor cells from a stem cell derived from neural tissue or non-neural tissue.

Applicants have also provided herewith a declaration under 37 CFR 1.132 signed by the inventors, which provides additional support for enablement of the invention. More particularly, the data support the use of the compounds of the present invention to promote the growth and differentiation of neuronal progenitor cells. In addition, the data support the previously unexpected finding that neural progenitor cells can be obtained from neural tissue (embryonic brain tissue) and non-neural tissue (bone marrow). There have been no previous studies reported prior to the inventors' own work that have demonstrated the isolation of neuronal stem cells or progenitor cells from a non-neural environment such as the bone marrow. Furthermore, there have been no other reports that a small molecule could have such a dramatic effect on the growth and differentiation of neuronal precursor cells from neural and non-neural tissue. Based on the amendments to the claims and to the supportive data presented in the declaration provided, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112.

The Examiner alleges that undue experimentation would be required to practice the invention as claimed because of the scope of compounds embraced. Applicants respectfully traverse. As regards the genus of compounds claimed, Applicants submit that a skilled artisan would be able to use the structure of the specific compound tested in the present application to develop analogs (such as those taught by the instant application) having similar biological activity. It would be expected that other compounds having a similar structure would have similar biological activity. Given the methods provided in the present application, making and screening such compounds constitutes nothing more than routine experimentation. The law is clear that a significant amount of experimentation is allowed before the threshold is crossed to undue experimentation. *See, In re Wands,* 858 F.2d 731 (Fed. Cir. 1988). Applicants submit that routine screening for similar compounds that promote nerve cell growth or differentiation could routinely be performed by the skilled artisan.

As noted in several of the abstracts provided to the Examiner along with the previous office action, the transplantation of neural precursor cells into injured or diseased animals results in recovery of neuronal function, with the type of functional recovery defined by the model in which the cells were tested. For example, Chiba et al, note that motoneuron-enriched neural progenitor cells obtained by culturing mouse embryonic stem cells with retinoic acid were transplanted into hemiplegic mice, which resulted in improvement of motor function in these mice. Furthermore, Parati et al. demonstrate that intrastriatal engraftment of neural stem cells gives rise to dopaminergic-like neurons which results in long lasting functional recovery in the 6HODA model for Parkinson's disease. In addition, Riess et al. demonstrate that transplanted neural stem cells survive, differentiate and improve neurological motor function in a mouse model of traumatic brain injury. And finally, Zhao et al. demonstrate that human bone marrow stem cells exhibit neural phenotypes and are capable of ameliorating neurological deficits after grafting into the ischemic brain of rats. In particular, these stem cells having neural phenotypes were able to restore sensorimotor function after experimental stroke.

It is apparent from the literature presented that neural stem/precursor cells are capable of restoring neuronal function in various models of neurodegenerative diseases and conditions, including traumatic brain injury, spinal cord injury, stroke and

Parkinson's disease. Accordingly, the compounds of the present invention promote neural stem/precursor cell proliferation as shown by the expression of neural stem/precursor cell markers, such as eNCAM, MAP II, β-tubulin, nestin, NF and NF-PO_4. Therefore, it follows that due to the profound effect of the compounds of the present invention on induction of neural stem cell/precursor cell growth, these compounds would be effective in restoration of neuronal function upon either direct administration of the compound to the mammal having experienced a traumatic brain or spinal cord injury or other neurodegenerative disease which results in neuronal dysfunction, or administration of bone marrow cells (as a source of stem cells) obtained from animals having been administered one of the compounds of the present invention. One of skill in the art would be aware of the potential neuronal functional recovery that may be attributed to administration of such compounds, whether it be recovery of motor function or cognitive function. Due to the pluripotent nature of the neuronal stem/precursor cells induced by the compounds of the present invention, restoration of multiple neuronal functions would be expected and these functions would vary depending upon the particular animal model used. Withdrawal of the rejection is respectfully requested.

Claim Rejections under 35 U.S.C. §112, second paragraph

Claims 57-58 are rejected under 35 U.S.C. 112, second paragraph as being incomplete for omitting essential steps, in particular, the omitted steps of collecting bone marrow cells from a first mammal and delivering them to a site of injury in the first or a second mammal. The claim has been amended to recite the missing step. Accordingly, withdrawal of the rejection is respectfully requested.

Rejections Under 35 USC § 102(b)

The Examiner has rejected claims 8-12, 19-23, 57, 67 and 69-72 under 35 USC § 102(b) as being anticipated by Nair et al. (U.S. Patent No. 4,965,284).

Applicants respectfully traverse the Examiner's rejection for the following reasons. The instant application teaches methods for promoting neural cell growth and differentiation comprising administering to a mammal a composition containing a compound selected from a genus of compounds, wherein said administering is effective

to promote the growth or differentiation of neuronal cells. Furthermore, these neural precursor cells may be identified on the basis of expression of one or more proteins such as those selected from the group consisting of : eNCAM, MAP II, β-tubulin, nestin, NF and NF-PO_4. In addition, the present application teaches methods for promoting recovery of cells expressing neuronal cell markers after injury to the neuronal cells through use of a compound from this genus. The instant application further teaches a method for promoting growth or differentiation of neural precursor cells comprising administering to a first mammal a neural growth promoting effective amount of a composition, collecting bone marrow cells from the first mammal and delivering them to a site of injury in the first mammal or in a second mammal; wherein the composition comprises the compound from the genus described. Furthermore, the administering is effective to promote the expression of one or more neuronal cell proteins such as those selected from the group consisting of : eNCAM, MAP II, β-tubulin, nestin, NF and NF-PO_4. The present application further teaches a method for treating injury to neuronal cells comprising exposing said cells to an effective amount of a composition containing one of the compounds of the genus described, wherein said administering is effective to promote the neuronal cell expression of one or more proteins such as those selected from the group consisting of : eNCAM, MAP II, β-tubulin, nestin, NF and NF-PO_4. The injury to neuronal cells may be the result of surgery, radiation therapy, chemotherapy or excititoxic agents.

Nair et al. teach the use of the claimed compounds for modulating the immune system and for stimulating proliferation and differentiation of **blood cell progenitors**, and for enhancing the activity of **immune cells** and/or immunoregulatory proteins. The Examiner asserts that Nair et al is silent with respect to "the tissue is of neuronal origin and the method is for promoting neural expression"; "the administration is effective to promote the neural expression of one or more proteins selected from the group consisting of eNCAM, MAP II, beta tubulin, nestin, NF and NF-PO4"; Promoting recovery of behavioral function of neurons after a decrease in neural function" and "promoting regeneration of neural precursor cells". However, the Examiner alleges that these properties are deemed to be inherently presented in the Nair reference.

Applicants respectfully traverse the Examiner's rejection and assert that in order

for a rejection under 35 U.S.C. 102(b) to be proper, the reference(s) must teach each and every element of the invention as claimed. Applicants assert that Nair et al. do not teach the methods of the present invention as currently claimed and that there are distinct differences between the teachings of Nair et al. and the present application.

For example, Nair et al. **do not teach or suggest** the use of this genus of compounds for growth and differentiation of neural precursor cells. Furthermore, Nair et al. **do not teach or suggest** that this genus of compounds could be used to treat neuronal precursor cells obtained from **neural tissue** or non-neural tissue to result in growth and differentiation of a population of neuronal cells having cell surface markers characteristic of neuronal precursor cells. Moreover, Nair et al. **do not teach or suggest** the use of this genus of compounds for treating injury to neuronal cells. Nair et al. provide no teaching as to how one can obtain neural tissue for treatment with the compounds of this genus. Nor do Nair et al. **teach or suggest** how one can utilize the neuronal stem cells obtained from the bone marrow to treat a mammal that has experienced a contusion to the spinal cord.

Accordingly, Applicants assert that Nair et al. **do not** teach or suggest the present invention as currently claimed. Nair et al. do not teach or suggest the methods of the current invention for treating neuronal cell injuries by stimulating growth and differentiation of **neuronal** stem cells, nor do Nair et al. teach how one may utilize these compounds for treating injury to neuronal cells or tissue. Nair et al. only teach the use of this genus of compounds for treating disorders in which the **hematopoietic** stem cell system is compromised, such as in cancer patients whereby the chemotherapy or irradiation therapy destroys hematopoietic stem cells, thus leading to a decrease in peripheral blood cell counts, resulting in neutropenia and susceptibility to infections following such therapies.

Applicants further assert that the rejection under 35 U.S.C. § 102(b) is improper in that the Nair et al reference is a non-enabling reference. As stated in In re Donohue, 766 F.2d 531, 533, 226 USPQ 619, 621 (Fed. Cir. 1985):

> It is well settled that prior art under 35 U.S.C. § 102(b) must sufficiently describe the claimed invention to have placed the public in possession of it. Accordingly, even if the claimed invention is disclosed in a printed publication, that disclosure

will not suffice as prior art if it was not enabling. It is not, however, necessary that an invention disclosed in a publication shall have actually been made in order to satisfy the enablement requirement.

For example, Applicants assert that Nair et al. do not teach or suggest the use of the compound of the present invention for promoting the growth or differentiation in neuronal precursor cells.

In light of the foregoing claim amendments and arguments, Applicants respectfully request withdrawal of the rejection.

Fees

No fees are believed to be necessitated by the present response. However, should this be in error, the Commissioner is hereby authorized to charge any fees, or credit any overpayment, to Deposit Account No. 11-1153.

Conclusion

Applicants believe that the foregoing amendments to the claims place the application in condition for allowance. Withdrawal of the rejections and objections is respectfully requested. If a discussion with the undersigned will be of assistance in resolving any remaining issues, the Examiner is invited to telephone the undersigned at (201) 487-5800, ext. 118, to effect a resolution.

Respectfully submitted,

Veronica Mallon

Veronica Mallon, Ph.D.
Agent for Applicants
Reg. No. 52,491

KLAUBER & JACKSON
411 Hackensack Avenue
Hackensack, NJ 07601
Tel: (201) 487-5800

Attachments: Declaration under 37 CFR 1.132